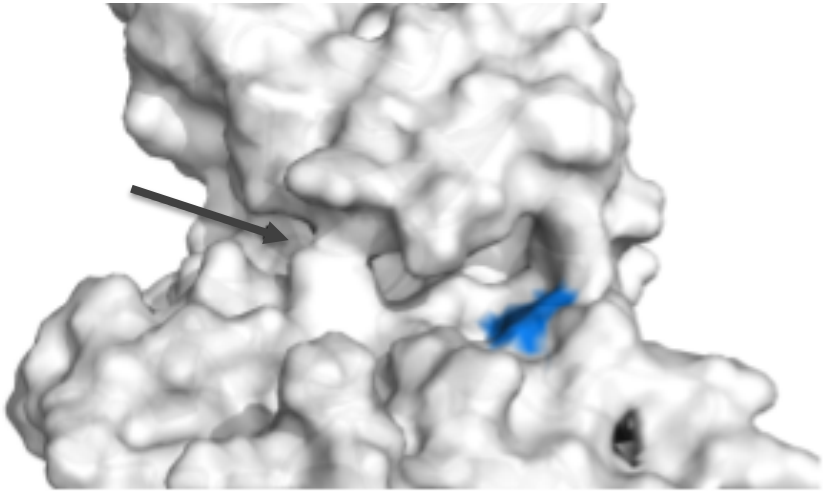
Small Molecule Discovery Partnership – *Project Overview*

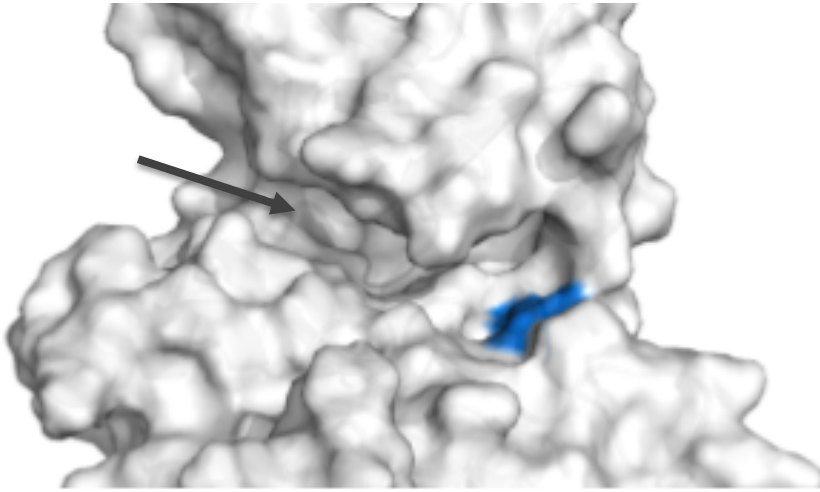
Outcomes

- **Analyzed Allosteric Effects of Ligand-Binding**
- **Identified New Potential Binding Sites**

- Phosphorylation
  - *Used* **Symmetric Homology Modeling with Ligand** *to model phosphorylation of apo and ligand-bound states based on known protein-ligand complexes*
- Allosteric effects
  - **Residue Pair Distance** *calculations (developed by Cyrus) were used to characterize specific binding modes and their allosteric effect*
- Conformational diversity
  - **Residue Pair Distance** *calculations was also used to characterize various states, and was sensitive enough to detect changes due to phosphorylation*
- Dynamic opening of binding pockets
  - *Potential (cryptic) binding sites were identified and opened through the* **Pocket Measure** *and* **Pocket Relax** *protocols*
- More potent screening
  - **Replace Ligand** *rapidly docked a small-scale screen of ligands to potential binding sites away from the known ligand-binding site, allowing many more protein conformations to be considered than typical screens*



Starting Model of Kinase



Pocket Relax centered at blue residue